Complete Summary

GUIDELINE TITLE

Pre-conceptional vitamin/folic acid supplementation 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies.

BIBLIOGRAPHIC SOURCE(S)

Wilson RD, Johnson JA, Wyatt P, Allen V, Gagnon A, Langlois S, Blight C, Audibert F, Desilets V, Brock JA, Koren G, Goh YI, Nguyen P, Kapur B, Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada. Pre-conceptional vitamin/folic acid supplementation 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies. J Obstet Gynaecol Can 2007 Dec;29(12):1003-13. [99 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Neural tube defects and other congenital anomalies

GUIDELINE CATEGORY

Prevention
Screening

CLINICAL SPECIALTY

Obstetrics and Gynecology
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide information regarding the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other congenital anomalies, so that physicians, midwives, nurses, and other health care workers can assist in the education of women in the pre-conception phase of their health care

TARGET POPULATION

Women of reproductive age

INTERVENTIONS AND PRACTICES CONSIDERED

Advise women about the benefits of:

- Folic acid
- Multi-vitamin supplement
- Healthy diet

MAJOR OUTCOMES CONSIDERED

- Maternal/fetal health outcomes
- Vitamin B_{12} deficiency
- Incidence of neural tube defects and congenital anomalies

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Medline, PubMed, and Cochrane Database were searched for relevant English language articles published between 1985 and 2007. The previous Society of Obstetricians and Gynaecologists of Canada (SOGC) Policy Statement of November 1993 and statements from the American College of Obstetrics and Gynecology and Canadian College of Medical Geneticists were also reviewed in developing this clinical practice guideline.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort (prospective or retrospective) or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

* Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classification of Recommendations*

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

I. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline was prepared by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada and The Motherisk Program, The Hospital for Sick Children Toronto, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The quality of evidence (**I-III**) and classification of recommendations (**A-E, I**) are defined at the end of the "Major Recommendations."

1. Women in the reproductive age group should be advised about the benefits of folic acid in addition to a multivitamin supplement during wellness visits (birth control renewal, Pap testing, yearly examination) especially if pregnancy is contemplated. **(III-A)**
2. Women should be advised to maintain a healthy diet, as recommended in *Eating Well With Canada's Food Guide* (Health Canada). Foods containing excellent to good sources of folic acid are fortified grains, spinach, lentils, chick peas, asparagus, broccoli, peas, brussels sprouts, corn, and oranges. However, it is unlikely that diet alone can provide levels similar to folate-multivitamin supplementation. **(III-A)**
3. Women taking a multivitamin containing folic acid should be advised *not* to take more than *one daily dose* of vitamin supplement, as indicated on the product label. **(II-2-A)**
4. Folic acid and multivitamin supplements should be widely available without financial or other barriers for women planning pregnancy to ensure the extra level of supplementation. **(III-B)**
5. Folic acid 5 mg supplementation will not mask vitamin B_{12} deficiency (pernicious anemia), and investigations (examination or laboratory) are not required prior to initiating supplementation. **(II-2-A)**
6. The recommended strategy to prevent *recurrence* of a congenital anomaly (anencephaly, myelomeningocele, meningocele, oral facial cleft, structural heart disease, limb defect, urinary tract anomaly, hydrocephalus) that has been reported to have a decreased incidence following preconception / first trimester folic acid +/- multivitamin oral supplementation is planned pregnancy +/- supplementation compliance. A folate-supplemented diet with additional daily supplementation of multivitamins with 5 mg folic acid should begin at least three months before conception and continue until 10 to 12 weeks post conception. From 12 weeks post conception and continuing throughout pregnancy and the postpartum period (4–6 weeks or as long as breastfeeding continues), supplementation should consist of a multivitamin with folic acid (0.4–1.0 mg). **(I-A)**
7. The recommended strategy(ies) for primary prevention or to decrease the incidence of fetal congenital anomalies will include a number of options or treatment approaches depending on patient age, ethnicity, compliance, and genetic congenital anomaly risk status.
    - **Option A**: Patients with no personal health risks, planned pregnancy, and good compliance require a good diet of folate-rich foods and daily supplementation with a multivitamin with folic acid (0.4–1.0 mg) for at least two to three months before conception and throughout pregnancy and the postpartum period (4–6 weeks and as long as breastfeeding continues). **(II-2-A)**
    - **Option B**: Patients with health risks, including epilepsy, insulin dependent diabetes, obesity with body mass index (BMI) >35 kg/m^2, family history of neural tube defect, belonging to a high-risk ethnic group (e.g., Sikh) require increased dietary intake of folate-rich foods and daily supplementation, with multivitamins with 5 mg folic acid, beginning at least three months before conception and continuing until 10 to 12 weeks post conception. From 12 weeks post-conception and continuing throughout pregnancy and the postpartum period (4–6

weeks or as long as breastfeeding continues), supplementation should consist of a multivitamin with folic acid (0.4–1.0 mg). **(II-2-A)**

- **Option C**: Patients who have a history of poor compliance with medications and additional lifestyle issues of variable diet, no consistent birth control, and possible teratogenic substance use (alcohol, tobacco, recreational non-prescription drugs) require counselling about the prevention of birth defects and health problems with folic acid and multivitamin supplementation. The higher dose folic acid strategy (5 mg) with multivitamin should be used, as it may obtain a more adequate serum red blood cell folate level with irregular vitamin / folic acid intake but with a minimal additional health risk. **(III-B)**

8. The Canadian Federal Government could consider an evaluation process for the benefit/risk of increasing the level of national folic acid flour fortification to 300 mg/100 g (present level 140 mg/100 g). **(III-B)**
9. The Canadian Federal Government could consider an evaluation process for the benefit/risk of additional flour fortification with multivitamins other than folic acid. **(III-B)**
10. The Society of Obstetricians and Gynaecologists of Canada will explore the possibility of a Canadian Consensus conference on the use of folic acid and multivitamins for the primary prevention of specific congenital anomalies. The conference would include Health Canada/Congenital Anomalies Surveillance, Canadian College of Medical Geneticists, Canadian Paediatric Society, Motherisk, and pharmaceutical industry representatives.

Definitions

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort (prospective or retrospective) or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Classification of Recommendations**

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

I. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

**Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Promoting the use of folic acid and a multivitamin supplement among women of reproductive age will reduce the incidence of birth defects.

POTENTIAL HARMS

- Multivitamins should have vitamin A as beta-carotene rather than as retinol. Excess retinol (10 000 IU; 3300 RE) on a daily basis may cause birth defects. For this reason, women should *not* take more than one daily dose, as indicated on the product label.
- The risk of toxicity from folic acid intake from supplements and/or fortified foods is low. It is a water soluble vitamin, so any excess intake is usually excreted in urine.
- Serum folate acid levels may be affected by the metabolism of other medications, including antineoplastic agents, epileptic medications, and other medications (See Table 3, "Interactions: Drugs and folic acid" in the original guideline document).

- Folic acid and multivitamin supplementation is possibly associated with an increased incidence of twins.
- There are some concerns about folic acid supplementation being associated with an increased risk of neoplasia or possible exacerbation of pre-existing colorectal cancer. Increased rates for colorectal cancer have been observed since food fortification was introduced in Canada and United States. This effect has not been proven but needs to be acknowledged.
- Allergic responses to folic acid are rare, but may include erythema, rash, itching, general malaise, and bronchospasm.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Wilson RD, Johnson JA, Wyatt P, Allen V, Gagnon A, Langlois S, Blight C, Audibert F, Desilets V, Brock JA, Koren G, Goh YI, Nguyen P, Kapur B, Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada. Pre-conceptional vitamin/folic acid supplementation 2007: the use of folic acid in combination with a multivitamin supplement for the prevention of neural tube defects and other

congenital anomalies. J Obstet Gynaecol Can 2007 Dec;29(12):1003-13. [99 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Dec

GUIDELINE DEVELOPER(S)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

SOURCE(S) OF FUNDING

Society of Obstetricians and Gynaecologists of Canada

GUIDELINE COMMITTEE

Society of Obstetricians and Gynaecologists of Canada Genetics Committee
The Motherisk Program

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada Web site.

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 9, 2009. The information was verified by the guideline developer on March 25, 2009.

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